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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/840,197	05/06/2004	Christopher J. Godfrey	VPI/03-117 US	7233

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EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	**PAPER NUMBER**
1631	
MAIL DATE	**DELIVERY MODE**
11/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/840,197	GODFREY ET AL.	
	Examiner	Art Unit	
	Karlheinz R. Skowronek	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *7,10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group I (claims 1-9) and species A: C_{max} and B: clearance, in the reply filed on 10 September 2007 is acknowledged.

Claims 7 and 10-11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention or species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10 September 2007.

Claim Status

Claims 1-11 are pending.

Claims 7 and 10-11 stand withdrawn as being directed to a non-elected invention.

Claims 1-6 and 8-9 are being examined.

Specification

The use of the trademarks PHARSIGHT TRIAL SIMULATOR (specification, p. 9) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-9 are drawn to a process. A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). The instant claims do not result in a physical transformation, thus the Examiner must determine if the instant claims include a useful, concrete, and tangible result.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, and substantial. For a claim to be "concrete," the process must have a result that is reproducible. For a claim to be "tangible," the process must produce a real world result. Furthermore, the claim must be limited only to statutory embodiments.

Claims 1-9 do not require production of a tangible result in a form that is useful to the user of the process. The claims are drawn to method of determining the distribution of an outcome following the administration of a compound that comprises the steps of using nonlinear mixed effects modeling to generate plurality of values and standard errors; inputting the plurality of values and errors to a stochastic pharmacokinetic model;

and generating a distribution of the outcome. The claims do not recite a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (British Journal of Clinical Pharmacology, Vol. 50, No. 2, p. 125-134, 2000) in view of Claret et al. (Journal of Pharmacokinetics and Pharmacodynamics, vol. 28, No. 5, p. 445-463, 2001).

The claims are directed to a method that determines a value and standard error for each of a plurality of pharmacokinetic parameters by applying nonlinear mixed effects modeling; inputting one of the determined pharmacokinetic parameters as a random variable in a stochastic pharmacokinetic model and determining an outcome distribution. In some embodiments the allometric parameter is a pharmacokinetic parameter. In some embodiments the pharmacokinetic parameter is CL (clearance) or V (volume of distribution) that is scaled allometrically.

Anderson et al. shows a method of estimating pharmacokinetic parameters using a nonlinear mixed-effects model (p. 127, col. 1). Anderson et al. shows the

pharmacokinetic parameters were standardized using an allometric scaling model (p. 127, col. 2). Anderson et al. shows the allometric values are used as an input in a pharmacokinetic model (p. 127, col. 2). Anderson et al. shows the pharmacokinetic model simulates the administration of a compound to a human and produces a distribution of an outcome (figure 6). In an embodiment Anderson shows the Cl and V are scaled allometrically (p. 127, col. 2).

Anderson et al. does not show a stochastic pharmacokinetic model.

Claret et al. shows a stochastic pharmacokinetic model (p. 447). Claret et al. shows that a stochastic pharmacokinetic model has the advantage of being flexible and better ability to model compartment and mixing heterogeneity (p. 446). Claret et al. suggests that stochastic pharmacokinetic modeling is suitable for simulations (p. 458).

It would have been obvious to one of skill in the art to modify the method of using the results of non-linear mixed-effects modeling in pharmacokinetic modeling of Anderson et al. with the stochastic pharmacokinetic model of Claret et al. because Claret et al. shows a stochastic pharmacokinetic model has the advantage of being flexible and better ability to model compartment and mixing heterogeneity.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. in view of Claret et al. as applied to claims 1 and 8-9 above, and further in view of Best et al. (Journal of Pharmacokinetics and Biopharmaceutics, Vol. 23, No. 4, p 407-435, 1995).

The claims are directed to a method that determines a value and standard error for each of a plurality of pharmacokinetic parameters by applying nonlinear; inputting one of the determined pharmacokinetic parameters as a random variable in a stochastic pharmacokinetic model and determine an outcome distribution. In some embodiments, the allometric parameter is designated a random variable with a probability density in the stochastic model. In some embodiments, the random variable has a mean equal to the allometric parameter and a standard deviation equal to the standard error of the allometric parameter. In some embodiments, the probability density corresponds to a normal or lognormal distribution.

Anderson et al. in view of Claret et al. as applied to claims 1 and 8-9 above shows a method of determining an outcome using a stochastic pharmacokinetic model.

Anderson et al. in view of Claret et al. as applied to claims 1 and 8-9 above do not teach embodiments in which the allometric parameter is designated as a random variable with a probability density; the random variable has a mean equal to the allometric parameter and a standard deviation equal to the standard error of the allometric parameter; and the probability density corresponds to a normal or lognormal distribution.

Best et al. shows a method of estimating population pharmacokinetics. Best et al. shows the allometric parameter is designated a random variable with a probability density in the stochastic model (p. 410). Best et al. shows the random variable has a mean equal to the allometric parameter and a standard deviation equal to the standard error of the allometric parameter (p. 421). Best et al. shows the probability density

corresponds to a normal or lognormal distribution (p. 426). Best et al. shows the method is able to estimate models of considerable complexity without suffering from numerical instability (p. 430).

It would have been obvious to one of skill in the art to modify the method of determining an outcome using a stochastic pharmacokinetic model described by Anderson et al. in view of Claret et al. as applied to claims 1 and 8-9 above with the estimation pharmacokinetic parameters having associated probability densities of Best et al. because Best et al. shows the advantageous ability to estimate models of considerable complexity without suffering from numerical instability.

Claims 1 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. in view of Claret et al. as applied to claims 1 and 8-9 above, and further in view of Gomeni et al. (Drug Information Journal, Vol. 35, p. 1047-163, 2001).

The claims are directed to a method that determines a value and standard error for each of a plurality of pharmacokinetic parameters by applying nonlinear; inputting one of the determined pharmacokinetic parameters as a random variable in a stochastic pharmacokinetic model and determine an outcome distribution. In an embodiment, the outcome is C_{max}.

Anderson et al. in view of Claret et al. as applied to claims 1 and 8-9 above shows a method of determining an outcome using a stochastic pharmacokinetic model.

Anderson et al. in view of Claret et al. as applied to claims 1 and 8-9 above do not show an outcome that is C_{max}.

Gomeni et al. shows the outcome is C_{max} (p. 1053, col. 2). Gomeni et al. shows that C_{max} is the maximum dosage that safely can be administered (p.1057, col. 2).

It would have been obvious to one of skill in the art to modify the method of determining an outcome using a stochastic pharmacokinetic model described by Anderson et al. in view of Claret et al. as applied to claims 1 and 8-9 above with determining a an outcome that is C_{max} of Gomeni et al. because Gomeni et al. shows C_{max} is the maximum dosage that safely can be administered.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karlheinz R. Skowronek whose telephone number is (571) 272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

14 November 2007

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